Extracellular Matrix and the Hair Growth Cycle

Andrew G. Messenger
Department of Dermatology, Royal Hallamshire Hospital, Sheffield, U.K.

In many mammals, synchronicity between hair-growth cycles in adjacent follicles results in the phenomenon of moulting. The timing of the moult and the duration of the phases of the hair-growth cycle may be influenced by environmental and systemic factors such as changes in photoperiod and a variety of circulating hormones. However, it is clear that local factors are involved in regulating the cycle as (i) the moult spreads as a wave over the skin and does not affect all follicles simultaneously and (ii) follicles transplanted from one body site to another remain in phase with the donor site for a prolonged period. Systemic factors, of which pregnancy is perhaps the best example, may synchronize hair-growth cycles in humans. There is also evidence that human hair retains vestiges of seasonal variation in growth. However, under normal circumstances, human follicles cycle independently of their neighbors. The success of hair transplantation demonstrates the importance of local control mechanisms in human hair follicles. Moreover, the retention of donor site characteristics by individually transplanted follicles suggests that control resides at the level of the follicle itself.

The molecular mechanisms responsible for initiating and terminating anagen and for determining their timing are unknown. However, there is substantial evidence to show that the mesenchyme-derived components of the hair follicle, comprising the dermal papilla and the connective tissue sheath, are responsible for inducing and maintaining epithelial differentiation in the hair bulb matrix. This is analagous to the embryonic situation where development of follicular epithelium is dependent upon (as yet undefined) signals from the mesenchyme. The cellular population of the dermal papilla is thought to remain fairly constant throughout successive hair-growth cycles, although proliferative activity probably occurs in dermal papilla vasculature during anagen. However, major changes take place in the morphology of dermal papilla cells and in the composition and volume of the extracellular matrix (ECM). During anagen, dermal papilla cells show ultrastructural evidence of synthetic activity and lie within an extensive ECM. The ECM diminishes during catagen and is minimal in the telogen follicle, where the dermal papilla consists of a tightly packed ball of cells. Human dermal papillae contain interstitial collagens and certain basement membrane proteins, such as laminin, type IV collagen, and heparan sulphate proteoglycan. These molecules are present throughout the hair-growth cycle [1,2] suggesting that they may have a structural role. The presence of basement-membrane proteins in the dermal papilla ECM has been documented in other species but, intriguingly, the papillae of rat pelage follicles contain little or no interstitial collagen [3]. Fibronectin has also been found in the dermal papilla during anagen but is lost as the follicle passes into telogen. Re-expression of fibronectin at the papilla-epithelial interface in early anagen correlates closely with the onset of proliferative activity in the secondary germ. Recent immunostaining studies have also demonstrated the presence of sulphated and unsulphated chondroitin in the dermal papilla and connective tissue sheath of anagen follicles but not in interfollicular dermis [1,3]. Staining for these glycosaminoglycans is lost as the follicle passes through catagen to telogen. Antibodies that recognise basement-membrane chondroitin sulphate proteoglycan also stain the dermal papilla ECM during anagen but not telogen [4]. Hypertrichosis may be a feature of disorders, such as pretibial myxedema and Hunter-Hurler syndrome, in which proteoglycans and their glycosaminoglycan side chains accumulate in the skin. It has also been shown that disturbance of proteoglycan metabolism in chick embryo skin disrupts normal feather development [5]. Together, these findings strongly suggest that proteoglycans are involved in the development of skin appendages and in mediating control of the hair-growth cycle.

Although we are at an early stage in understanding the role of ECM in hair growth, interactions with ECM are thought to be important in controlling structural organization, growth, and differentiation in a variety of tissues, for example, through binding of matrix constituents to specific membrane receptors (e.g., integrins, cell adhesion molecules), and localizing or filtering of cytokines and other bioactive molecules. The identification of such interactions in the hair follicle is an important target for future research.

Reprint requests to: Dr. A. G. Messenger, Department of Dermatology, Royal Hallamshire Hospital, Sheffield S10, U.K.

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